



The VA Parkinson Report

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A Newsletter for the Parkinson's Disease Research, Education and Clinical Centers
and The National VA Parkinson's Disease Consortium

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Novel Rescue Medications in Parkinson's Disease

Ian Walker, MD, Philadelphia PADRECC, Corporal Michael J. Crescenzo VAMC

As a neurodegenerative disorder, Parkinson's disease (PD) is known to progress through multiple distinct phases, characterized by the development of motor and non-motor symptoms that increase in severity over time. These phases are believed to correspond to progressive degeneration of nigrostriatal dopaminergic pathways and accompanying accumulation of malformed alpha-synuclein in the form of Lewy bodies. As the cardinal motor features of resting tremor, rigidity, and bradykinesia arise, patients are often started on some form of dopaminergic replacement therapy. During this early clinical phase of PD, such therapy usually delivers control of symptoms with tolerable side effects. Over time, however, greater denervation of dopaminergic circuitry and alterations in dopamine receptor sensitivity result in increasingly difficult to control motor symptoms accompanied by fluctuating responses to treatment. These motor fluctuations are generally referred to as "On" and "Off" states that can produce distress due to a symptomatic "wearing off" and accompanying non-motor symptoms such as anxiety, depression and panic attacks. At that point, more tailored and thoughtful medical regimens are implemented based on timing and description of symptoms. These enhanced regimens include increased frequency or extended formulations of oral carbidopa-levodopa, and adjunctive agents including MAO-B inhibitors and COMT inhibitors to extend "On" times and reduce "Off" times.

In advanced patients, fluctuations can evolve into sudden changes between states, or "On-Off" phenomena. Due to their unpredictability, these events can be especially disabling, both during the daytime and at night. To rapidly return to the "On" state, multiple rescue therapies have been devised. These include the administration of "liquid" levodopa, consisting of a crushed formulation of regular or controlled-release levodopa dissolved in a beverage. While there is uncertainty as to its clinical benefit, due to ease of administration for those patients who can swallow it has been adopted as an intervention.

Another option to address severe and sudden "Off" periods is subcutaneous injection of apomorphine. A short acting dopamine agonist, apomorphine produces an effect within 5-15 minutes with duration of benefit lasting 45-90 minutes. Due to the potential to produce nausea, patients often take an antiemetic such as trimethobenzamide prior to administration. Multiple clinical trials have shown apomorphine to produce a rapid increase in UPDRS motor score during acute "Off" events and a reduced number of "Off" hours per day. Available in Europe and under review by the FDA, continuous infusions of apomorphine are now being utilized to produce a significant reduction in "Off" time for patients with persistent motor fluctuations refractory to oral or transdermal medication.

Novel Rescue Medications in Parkinson's Disease (continued)

Despite its efficacy, apomorphine has a limited duration of action and certain adverse effects such as development of subcutaneous nodules at injection site and need for antiemetic administration. As a result, efforts have been made to develop more convenient and non-invasive administration routes such as inhalational and sublingual that bypass intestinal absorption. There is an orally disintegrating form of carbidopa/levodopa (Parcopa), but it has not been shown to have a faster onset of action than standard carbidopa/levodopa.

Recently, attention has been focused on a novel levodopa inhalation powder, CVT-301, as a treatment for motor fluctuations in Parkinson's disease. Phase IIa and IIb trials were completed for this drug in 2014 and 2016 with a clinically significant improvement in UPDRS Part III score found within 10 minutes and present past 60 minutes post dose. Furthermore, patients taking CVT-301 self-reported a reduction in their daily duration of "Off" time.

Based on the success of these studies, a phase 3, double blind, placebo-controlled trial (SPAN-PD) was performed with results published earlier this year. The study randomized 339 levodopa-responsive patients to two treatment groups administered CVT-301 84mg or 60mg and to a placebo group. The study was conducted over a 12 week period with a primary endpoint of change in UPDRS Part III score 30 minutes post-dose, assessed at week 12 of the study. Total daily "Off" times and change in motor score at other time points post-dose were also collected as secondary endpoints. At 30 minutes post-dose, the mean improvement in Part III score in the treatment arms was found to be 9.8 compared to 5.9 in the placebo arm ($p < .009$), with a dose-dependent response. Review of other time points reiterated motor improvement starting at 10 minutes and lasting up to 60 minutes post-dose. An affiliated open-label study showed similar results after 4 weeks and 52 weeks. So far, the utility of CVT-301 in early morning "Off" periods remains unclear.

As a measure for therapy-related airway changes, pulmonary function testing performed on these subjects revealed no difference between the treatment and placebo groups. In these studies, cough has been reported as the most frequent side effect but has not impacted treatment.

Based on the promising results of these clinical trials, a new drug application for CVT-301 was filed by Acorda Therapeutics in February 2018 with subsequent FDA approval in December 2018 under the brand name Inbrija. The drug is administered in 42mg fine-powder capsules for a total dose of 84mg, with administration up to 5 times per day for "Off" periods..

While Inbrija is one of the first non-invasive treatments for motor fluctuations and for PD as a whole, there are currently multiple other drug candidates being investigated, with a sublingual form of apomorphine already under review by the FDA. Over time, the utility of these novel agents alongside current treatments will be better understood to allow for individualization and optimization of therapeutic regimens.

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Novel Rescue Medications in Parkinson's Disease (continued)

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Assessment and Management of Functional Movement Disorders

Dr. Joel Mack, Northwest PADRECC, VA Portland Health Care System

Functional (or *psychogenic*) movement disorders (FMDs) are syndromes characterized by abnormal movement symptoms that are distractible, inconsistent over time, and incongruent with known neurological ("organic") causes of movement disorder, however the symptoms are not feigned. They are relatively common disorders, being seen in 3-4% or more of patients presenting at movement disorders clinics, an estimate recently replicated in veterans at our Portland VA movement disorders clinic, with tremor being the most common phenomenological presentation. In 2006, FMDs were described as "a crisis for neurology" because of the dilemma they present in terms of etiology, diagnosis, underlying pathophysiology, treatment, and poor prognosis. Fortunately, there has been increased interest in FMDs and significant (albeit early) progress made in the field since that time, with ongoing research and greater understanding of pathophysiology and effective treatments. Physical therapy has been shown to be an effective treatment for FMD and this has resulted in successful treatment programs being established. FMDs are no longer considered a diagnosis of exclusion, with phenotype-specific diagnostic criteria based on neurological symptoms and signs having been proposed. While a history of psychological trauma is no longer required for FMD diagnosis, psychological disturbances remain important as risk factors for FMD, and there is evidence for the benefits of psychotherapy interventions in functional neurological disorders including FMD. For years there was reluctance on the part of both psychiatry and neurology to take ownership of FMD patients, but it is now evident that the most effective approach involves treatment across biopsychosocial domains with involvement of multiple disciplines tailored to the individual patient.

The Northwest PADRECC is in the process of establishing a multidisciplinary FMD clinic, an effort being led by neuropsychiatrist, Dr. Joel Mack. This will involve FMD diagnosis by movement disorders neurologists, physical therapy intervention for motor retraining, neuropsychiatric assessment and treatment of comorbid psychiatric disturbances, as well as a manualized psychotherapy intervention. FMDs have been a more prominent topic of education in the clinic, and movement disorders fellows and attending neurologists have become more comfortable with diagnosing FMD and delivering that diagnosis to the patient. The confident diagnosis of FMD and positive reinforcement that the symptoms will improve can be therapeutic for FMD patients and lays the foundation for successful treatment. While evidence for treatment approaches is growing, it will be important to establish reliability across FMD treatment centers (What is the best physical therapy approach or FMD patients? What elements of psychotherapy are most useful?), as well as to examine long-term outcomes. We will be translating an evidence-based psychotherapy workbook for psychogenic non-epileptic seizures for use in FMD specifically and examining its efficacy as a complementary/additional treatment to physical therapy. We hope that establishing multidisciplinary PADRECC FMD clinic will serve as a model for the delivery of FMD treatment within the VA system.

Rhythm N Dance

Dawn Parker-Korinek, OTR/L & Bethany Riedel, MT-BC, Tomah VAMC

The *Tomah VA* Occupational, Music, and Speech Therapy departments have developed a Therapeutic Movement group we call *Rhythm N Dance*. This group was developed after two Nurse Practitioner students conducted a thesis study last summer involving Veterans with Parkinson disease. The group was well attended and the Veteran's requested to continue with this type of programming.

Our VA established a *Ready, Steady, Go!* Balance and home safety class in which Veteran's can identify different electives to participate in to continue their fitness and balance program. One of the offerings is the *Rhythm N Dance* class.

From this we have developed a set of measures to base our goals, these include: Single Limb Stance Test, Five Times Sit to Stand, Timed Get Up and Go (TUG), and Gait Speed. These measures are done either by a Physical Therapist who is referring the Veteran or by the Veteran attending our *Ready, Steady Go!* Balance Class. Veteran's must have a neurological condition to participate.

Our present class is limited to 8 participants and their caregivers and runs for 8 weeks. We have had volunteers assist in the class. The class is 90 minutes. In each class we begin with seated warm ups, then progress to drumming, dancing the adapted tango, seated rhythmic movement with maracas, singing, followed by waltzing, then working at the bar on the wall practicing squatting, balance, tiptoe and weight shifting followed by a cool down and farewells.

We have completed one eight-week session with two Veteran's retesting the measures from which they both made statistically significant gains on almost all of the measures. We are now on our second group and the size of our group has doubled. We are presently allowing Veteran's to repeat the session as long as there is room for new attendees.

We have had a very positive response from Veteran's in the group, and their Personal Health Inventory (PHI) is consistently higher at the end of class than at the start of class.



Blue Water Navy Vietnam Veterans Act of 2019



The Blue Water Navy Vietnam Veteran Act of 2019 was signed into law on June 25, 2019 and goes into effect January 1, 2020. This new law affects Veterans who served on a vessel operating not more than 12 nautical miles seaward from the demarcation line of the waters of Vietnam and Cambodia as defined in Public Law 116-23. Veterans who state they meet the criteria of this law are eligible for the Agent Orange Registry, being on this registry does not verify eligibility for benefits. These Veterans may qualify for a presumption of service connection if they have a disease that is recognized as being associated with herbicide exposure, *Parkinson's disease* is on this recognized list. For more information Veterans

should call the VA's toll free number, 1-800-827-1000 or visit the VA Blue Water Navy Agent Orange website: <https://www.publichealth.va.gov/exposures/agentorange/locations/blue-water-veterans.asp>

Philadelphia PADRECC Update

Clinical Update

Expansion of Telehealth: Dr. Daniel Weintraub of the Philadelphia PADRECC, in collaboration with and funded by the National Telemental Health Center based out of New Haven, CT, is providing initial psychiatric consult services to the Bronx, Northport, Albuquerque, San Diego, Tampa, Ann Arbor, Dallas and Portland (OR) VAMCS for patients with PD and psychiatric-cognitive symptoms. Psychiatric symptoms in patients with PD have a large impact on quality of life and managing these symptoms can be difficult and should be done by a subject matter expert. Both providers and Veterans are happy with the service and Dr. Weintraub is in the process of expanding the service to other VAMCs. Please contact him at daniel.weintraub@va.gov if you think your PD patients could benefit from such a service.

The Philadelphia PADRECC currently provides telehealth services to 7 VA Medical Centers and 16 CBOCs within VISN's 2 and 4 and this year added the Delaware Valley Veteran State Home to the list. Telehealth is used to provide consultative services, follow up care, DBS stimulation adjustments, and medication management. *VA Video Connect* into the home is a modality used to reach Veterans who find traveling to a VAMC or a CBOC too difficult and is a great tool for clinicians to follow up on the most vulnerable Veterans.



Staff Update: Eileen Hummel, MSN, CRNP: Eileen Hummel-PADRECC Clinical Nurse Coordinator completed her Master of Science in Nursing program and is now a licensed Nurse Practitioner. Eileen will function in the role of a Nurse Practitioner in The Philadelphia PADRECC and will continue to collaborate with the Attending Neurologists.

Education Update

11th PADRECC/MIRECC Symposium on Neurodegenerative Diseases: Update on Psychiatric and Cognitive Complications in Parkinson's Disease (PD) and Dementia with Lewy Bodies (DLB): The Philadelphia PADRECC in collaboration with the Philadelphia MIRECC hosted this CME program on **March 29, 2019** to continue the practice of delivering an informative symposium for clinicians and clinical researchers. There were approximately 92 VA and Non-VA healthcare professionals who attended this symposium.

Veterans Empowered Through Art: The Six Week Selfie Project: On April 24, 2019, the Corporal Michael J. Crescenz VAMC presented *Veterans Empowered Through Art: The Six Week Selfie Project*, an exhibit by the Philadelphia Museum of Art in partnership with the Veterans Empowerment Center and the Philadelphia VA PADRECC. This exhibit chronicled the work of 18 Veterans who were part of *The Six Week Selfie Project*, a class where students explored artistic expression through tours of the museum as well as workshops in visual arts and writing. Highlights of the exhibition included preliminary portraits with no instruction, completed self-portraits done in about 12 hours, samples of creative writing and poetry, and personal photos of the Veterans during their time of service. There were both live and video presentations of participants sharing their experiences as well as a presentation of a group poem and a personal poem. Nine PADRECC Veterans participated in this exhibition.



Community Outreach: Clinical Staff continue to attend local community health fairs and present at local support groups providing information and education on the PADRECC program and services available as well as information on topics related to PD.

Philadelphia PADRECC Update (continued)

Patient & Caregiver Support Group Program: This program runs from April-December and meets once a month for one hour to provide support and education on topics related to Parkinson's Disease. To increase accessibility, some groups are broadcasted to two local CBOCs using tele-health technology.

Research Update

Exercise and Parkinson's Disease: Dr. Morley is conducting a study supported by the VA Rehabilitation R&D service to study exercise as a therapy to improve symptoms and, potentially, slow disease progression in PD. Patients with early PD are randomized to exercise (aerobic walking up to 5 times per week) or control groups. Effects on motor symptoms and cardiovascular fitness are tested after 8 and 52 weeks while dopamine transporter SPECT scans are measured at baseline and after 52 weeks. This study will continue to recruit new patients through the end of 2020.

Dr. Sneha Mantri, former PADRECC Fellow, and Dr. Morley continue to study physical activity habits of people with PD. Participants were asked to complete questionnaires to assess exercise and activity habits, attitudes about exercise, sleep, mood, memory, and other symptoms. Only one in five meet American Heart Association recommended physical activity (20-30 minutes of moderate to vigorous activity, 2-3 times per week). Active Veterans score higher on cognitive tests, have fewer PD-related symptoms, and enjoy a better quality of life. By understanding physical activity habits, we can better design exercise programs to increase activity. A new study is examining the use of wearable technologies (Fitbit) to measure and improve physical activity in PD patients.

Medication-Induced Parkinsonism: Symptoms of PD can be mimicked by certain medicines that block dopamine—the major brain chemical missing in PD. Not everyone's symptoms improve after the medicines are switched or stopped, so it is possible that the medicines uncover very early PD in some cases. Dr. Morley's team is comparing medication-exposed patients with and without PD symptoms using questionnaires, physical exam, blood tests and a brain scan. Initial analyses published recently demonstrated that more than 20% of patients with drug-induced symptoms actually had underlying PD or a related disorder that was "unmasked" by the dopamine blocking drugs. Loss of sense of smell (as is seen in most PD patients) was the strongest predictor of an abnormal brain scan. Appearance of PD-like symptoms after treatment with a low dose of antipsychotic medication also predicted an abnormal scan suggesting that dopamine blocking drugs can act like a "stress test" for the brain.

The Immune System and Parkinson's Disease: Dr. Morley and the PADRECC are collaborating with a local biotech company (Longevity Biotech) on a project recently funded by the Michael J. Fox Foundation to study whether the immune system plays a role in PD. The team will recruit *pairs of patients and their caregivers* to study whether immune cells and other blood markers are different in PD and are associated with disease severity or other PD characteristics. This study has recruited 40% of its goal and will continue enrolling through the end of 2019.

Bacteria and Parkinson's Disease: Dr. Duda, in collaboration with Dr. Noam Cohen from the Ear Nose and Throat Department, continue to study how bacteria that colonize our body might contribute to the risk of PD. It has been shown that these bacteria are different in people with PD compared to people without PD. This study is trying to understand if there are genetic reasons why some people have certain types of bacteria in the hopes of developing new therapies in the future. Preliminary results confirm prior studies showing that participants with PD were more likely to be non-tasters of bitter compounds compared to participants without PD. Once recruitment is complete, they will examine differences in the genetics of the taste receptors and in the bacteria of the nose and gut between those with PD and those without.

Traumatic Brain Injury: Dr. Duda and his colleagues, Drs. Kacy Cullen, Isaac Chen and John Wolf, from the Department of Neurosurgery at the University of Pennsylvania, continue studies funded by the Rehabilitation Research and Development Service of the Department of Veterans Affairs to study the relationship between brain trauma and neurodegeneration. The researchers have published several studies that have shown how the brain reacts to trauma and how that could possibly lead to chronic neurodegenerative disease development. It is hoped that these studies will lead to treatments to prevent the development of these neurodegenerative diseases in Veterans and others who have suffered head injuries.

Neurorestoration in Parkinson's Disease: Dr. Duda and his colleagues Dr. Kacy Cullen and Isaac Chen from the Center for Neurotrauma, Neurodegeneration, and Restoration (CNNR) at the Crescenz VA Medical Center, continue to investigate whether one of the main brain pathways affected in PD, the nigrostriatal pathway, can be generated in a petri dish and transplanted in animal models to reverse the motor symptoms in PD. The success of their efforts to date have led to several publications and special recognition at several different scientific meetings and additional research grants to continue these studies. The team has been successful in implanting these bioengineered pathways into a rat model of PD and are now funded to do the same in pigs, which more closely resemble what would need to be achieved to begin trying this approach in humans.

Houston PADRECC Update

Houston's PADRECC is housed in the Michael E DeBakey VA Medical Center provides state of the art medical and surgical services to Veterans with Parkinson's disease and related movement disorders who reside in the South Central and Mid-Western United States. The area served by the Houston PADRECC includes all or parts of the following states: Texas, Louisiana, Mississippi, Oklahoma, Arkansas, Alabama, Florida, Kansas, Missouri, Indiana, Illinois, Wisconsin, and Kentucky (Houston PADRECC Consortium).

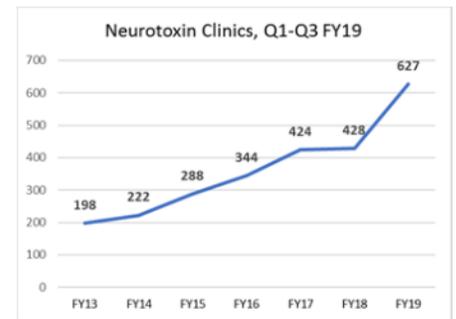
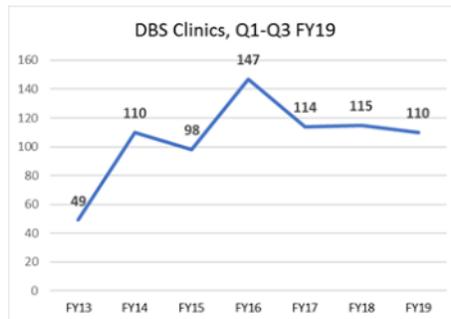
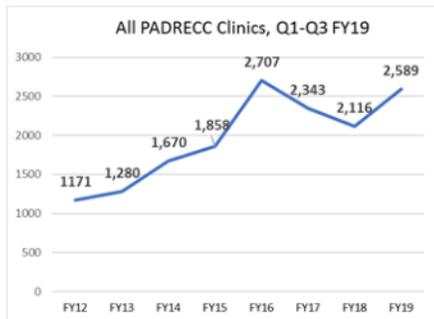
Consortium Update:

Per Deputy CMO of VISN 15 request, Topeka was removed as a consortium center in June 2019, from the National Consortium list due to shortage of neurologists. Topeka has been one of our consortium sites since 2009, Dr. Prasunamba Amaraneni was director, who has retired.

Clinical Update

Personnel shortage continues. Dr. Paolo Moretti's position, (one of our movement disorder specialists, who relocated to Utah in early FY18), is still vacant. Our administrative officer's position remains un-filled since 2017 due to SCS hiring freeze. We received some administrative support from the Neurology Care Line (NCL), since the above mentioned, however NCL's administrative officer retired in 4/2019 and her position is currently unfilled. Hence, Houston PADRECC is facing operational challenges given lack of dedicated administrative support, especially given increasing demands on our clinical services. As in years before, Houston PADRECC remained ahead of all other PADRECCs (single hospital comparison) with respect to patient encounters in this fiscal year.

There has been a total of 2,589 patient encounters through the end of the 3rd quarter of FY19, approximately **22%** more than the same time point in FY18. Activity in our procedure clinics i.e., **Deep brain stimulation** and **Neurotoxin injection** therapy clinics has decreased by **3.5%** and increased by **46%** respectively.



New Initiatives:

- Began talks with OT to provide therapy and adaptive equipment directly at the PADRECC clinics

Education Update

Houston PADRECC's Associate Director for Education position remains unfilled due to SCS hiring freeze. We have continued our 16 educational programs geared towards patients/caregivers, medical trainees and practicing healthcare providers. These include: 1) Clinic based patient/caregiver education, 2) Patient's monthly educational support group, 3) Patient and Caregiver educational conference (Educational Forums), 4) Collaborative Patient Educational Programs with Community groups, 5) Patient and Caregiver based educational newsletter (PADRECC Pathways), 6) Medical Staff's weekly educational conference, 7) Medical staff's monthly journal club, 8) Physicians' monthly Clinical Case Conference, 9) Medical staff's monthly inter-disciplinary surgical case discussion series, 10) Monthly Consortium based tele- educational meeting, 11) PADRECC based BCM neurology residents monthly elective rotation, 12) PADRECC's joint educational venture with Pharmacy residency training program, 13) In-patient medical student and medical residents hands on educational experience, 14) PADRECC physicians' lectures (including grand rounds, invited lectures) at the VA, BCM, national and international locations, 15) Contribution to the transmitter (e-newsletter) 16) Nurse lecture series.

Houston PADRECC Update (continued)

New Initiatives:

- In FY19, Dr. Sarwar began QI (quality improvement) lecture series geared towards our physicians to review latest guidelines for the management of different aspects of movement disorders. (once/month).
- Developed PADRECC based training program (including drafting a section on PADRECC based training for the Geriatric fellowship handbook) in collaboration with Geriatric Fellowship Program (Baylor College of Medicine, MED VAMC) for 2-4-week training of geriatric fellows at Houston PADRECC (1-2 fellows/FY).

Research Update

We currently have **11** active research projects. In FY19, we have continued recruitment in our Circadian Rhythm/ Sleep Study and screening subjects for a collaborative project with the GI department entitled “High Resolution Manometric Abnormalities of the Esophagus and Clinical Features of Gastroesophageal Reflux in Patients with Parkinson’s Disease”.

Renewal for our collaborative traumatic brain injury project has been submitted.

New Initiatives: (grants submitted and new collaborations)

- Rose Fulbright Academy of Distinguished Educators Educational grant (Baylor College of Medicine) to further the “Brain Health Initiative” was submitted in May 2019, Aliya I. Sarwar, MD
- Houston Alzheimer’s Disease Research Center Consortium, George R. Jackson, MD, PhD
- Integrated analysis of the metabolite and gut microbiome of tryptophan metabolism and sleep deficiency, Li Jiao, MD, PhD (PI), Sarwar, AI (Co-I)

Publications and other research presentations: (10/1/2018 – 06/30/2019)

ⓄAbstracts/posters = 13 (accepted or presented)

ⓄManuscripts = 6 (4 published, 2 in development)

Southeast/Richmond PADRECC Update

Clinical Update



New Neurosurgeon Joins Southeast/Richmond PADRECC

Dr. Paul Frederick Koch joined the Southeast PADRECC in 2018. He completed his residency training at the University of Pennsylvania, and a fellowship in Stereotactic and Functional Neurosurgery at Emory University. Dr. Koch’s clinical interests include the surgical treatment of epilepsy, stereotactic therapies for movement disorders and other conditions, including deep brain stimulation and lesioning, and the treatment of pain through open and neuromodulatory therapies. He also runs a basic science laboratory investigating traumatic brain injury, both the acute management and the long-term cognitive sequelae, including the development of post-traumatic epilepsy.

Telehealth Update: The Southeast PADRECC has a robust Telehealth program. In Fiscal 2018, 504 Veterans were seen utilizing Telehealth. For Fiscal 2019 Q1-Q3, 431 Veterans have been seen via Telehealth to date. We have also expanded our VA Video Connect program in which Veterans are evaluated at home by a PADRECC specialist using their own personal computing device. Telehealth is a useful tool for new consults, follow up care, medication adjustments and DBS pre-and postoperative evaluations and stimulation adjustments.

The Southeast PADRECC has a robust DBS telehealth clinic where Veterans who are interested in DBS but do not live locally, can be evaluated for surgery. This can be done through clinical video telehealth (CVT) from their local Community Based Outpatient Clinics or by utilizing VA Video Connect (VVC) from their homes. This technology is also used for follow-up DBS evaluations, if preferred by the Veterans, including yearly assessments and for assistance with DBS programming. All DBS patients undergo comprehensive preoperative physical and speech therapy evaluations and a tele-rehabilitation clinic has been developed to evaluate them postoperatively. A DBS tele-support group is offered several times per year where Veterans can call in utilizing the VA National Telecommunications System (VANTS).

Southeast/Richmond PADRECC Update (continued)

DBS Update: The Southeast PADRECC has an interdisciplinary DBS clinic including neurology, neurosurgery, neuropsychology and psychiatry, physical medicine and rehabilitation. Two neurosurgeons are available to perform this highly specialized procedure which is done using a frameless method of stereotaxy. Each month, on average, 8 DBS procedures are performed including lead and battery implantations and battery replacements.

The Southeast PADRECC DBS research efforts include improvements in the accuracy of the DBS procedure utilizing intraoperative imaging and recordings. Additionally, the Southeast PADRECC study team is involved in further refinements to frameless stereotaxy with the goal of promoting a more comfortable surgical experience. Other research interests include, but are not limited to, expanding the applications of neuro modulation to treat symptoms and diseases such as dementia in PD; understanding the role of neuronal signaling and their utility as stimulation parameters; optimizing electrode placement and stimulation parameters using EEG responses; analyzing the effect of lead location on outcome utilizing normalization software. The Southeast PADRECC is a study site for numerous DBS related clinical trials including, but not limited to the following:

- Accuracy of Targeting Subthalamic Nucleus vs Globus Pallidus and Clinical Implications
- Registry for the Advancement of Deep Brain Stimulation in Parkinson's Disease (RAD-PD)
- Safety and feasibility of deep brain stimulation of the nucleus basalis of Meynert to Improve cognitive functioning in Parkinson's disease dementia
- The Effect of Repetitive Transcranial Magnetic Stimulation of the Mouth Primary Motor Cortex on Parkinsonian Speech Dysfunction.
- Intraoperative O-Arm Guidance During Frameless Stereotactic Placement of Deep Brain Stimulators
- Physiological Brain Atlas Development

Education Update

Patient and Caregiver Support Group: The Parkinson's disease support group meets 8 times per year offering assorted topics related to PD. The goal of the group is to help Veterans with PD and their families learn how to adapt to the physical, emotional and psychosocial challenges associated with PD.

Community Outreach: Clinical staff present at different support groups around the state of Virginia as well as speak at professional conferences providing information on topics related to PD.

PD Rehab Hands on Workshop - GIVE PARKINSON'S DISEASE THE "SHAKE DOWN":

The Southeast PADRECC together with Physical Medicine and Rehabilitation held a Hands-On workshop on *Friday April 12, 2019* during PD Awareness Month. The event was well attended by our Veterans and patients with PD in the community. The purpose of the workshop was to demonstrate the importance of incorporating rehabilitation therapies i.e. Physical, Occupational, Speech, Recreational, Music and Kinesiotherapy into the treatment of patients with PD.

The workshop consisted of 7 stations. The participants rotated through the stations every 15 minutes. Each therapist set up their station with information and equipment pertinent to their specialty. Participants were able to experience numerous activities including painting, music expression, voice exercises, utilizing adaptive equipment, upper and lower body exercises, and tai chi. They were also able to visualize and use different types of equipment pertinent to the specialty. Patients and families left with knowledge of the different options available to assist them with challenges that are difficult to manage with medications alone.



Southeast/Richmond PADRECC Update (continued)

Upcoming APDA – Virginia Education Day – On *September 28, 2019*, several members of the Southeast PADRECC will participate in the PD Education Day for People and Families Living with PD. There will be educational presentations/panel on Understanding, Managing and Living with PD and breakout sessions with numerous topics presented including PD Research update, PD 101, Nutrition & PD, Exercise & PD and a Caregiver breakout session.

Research Update

Eye Movement Research in PADRECC: This long standing study was started approximately 10 years ago. Many thousands of subjects have been enrolled into the study, resulting in a massive data sample across the spectrum of movement disorders. Utilizing a 5 minute long data recording from an eye tracking device, the specific oculomotor parameters can be used to differentiate numerous neurological movement disorders. This project was funded for \$1M from the Michael J Fox foundation, with Dr. Gitchel serving as the local PI (VCU is lead site with Mark Baron MD as study PI, and Emory and University of Iowa are sub-sites). Preliminary results from the MJFF study are showing ~97.5% accuracy in diagnosing and differentiating PD and other movement disorders. As this data has become stronger over the years, Drs Gitchel and Baron and their university collaborator have applied for an international patent which is currently pending. Additionally, the intellectual property resulting from this research has been licensed to a company who is rapidly developing this into a commercially viable product which will be marketed as a clinical and *pre-clinical* biomarker for PD and other movement disorders. When the company announced the development of our product at CES, our product was awarded the Innovation Award for “Technology that will create a better world”. The product has been cleared by the FDA as a class 2 medical device

BOSS-PD, Urinary incontinence in PD: The Southeast PADRECC is a sub-site to a MERIT funded study out of the Atlanta GRECC and incontinence clinic. This study aims to determine the non-inferiority of pelvic floor muscle exercises to drug therapy that may cause cognitive slowing.

Bile Acids and Gut Microbiome: Locally funded with Dr. Bajaj as PI, investigating the microbiome of patients with cirrhosis. Patients with PD are being recruited as a secondary arm to the study due to their known gut motility and microflora changes.

Quantified Rigidity Monitor: This is a device that has been built in collaboration with the department of biomedical engineering at the local university. The device is a reliable, repeatable, quantifiable method to assess muscle rigidity in patients with PD. Funding has been applied for via the Innovator’s Network to finalize, validate and produce this device for multiple sites.

Northwest PADRECC Update

The Northwest PADRECC is comprised of the VA Portland Health Care System and the Puget Sound VAMC and consortium sites. The service area for the NW PADRECC is extensive including the VISN20 network of the Pacific Northwest (Oregon, Washington, and Alaska) and outside VISN20 consortium centers Montana, Wyoming, Idaho, Nebraska, South Dakota, and Iowa.

Clinical Update

Telehealth: The NW PADRECC Portland has a very active Telehealth clinic seeing 15-20 patients per month as both new evaluations, follow up care, and pre-DBS screening. The Portland telehealth clinic served 15 facilities outside of Portland, adding South Dakota to our telehealth region in FY19. The Portland PADRECC served areas outside of VISN20 in Montana, Wyoming, and South Dakota. In addition, the NW PADRECC is participating in the national telehealth clinic spearheaded by Dr. Daniel Weintraub of the Philadelphia PA PADRECC.

DBS: In FY19 Portland has completed 19 DBS surgeries and 21 battery changes. We are continuing to program veterans who come to us for the surgery from outside our VISN via telehealth with the local provider. This has saved multiple trips for these veterans back and forth to Portland.

Botox: Portland and Puget Sound continue to have very active Botox injection clinics. Portland injects over 150 individuals 3-4 times a year (500+ visits per year) and Puget Sound injects over 35 individuals (90+ visits per year).

Northwest PADRECC Update (continued)

Faculty Updates



After 30+ years of service at the Portland VA, **Steven Johnson, MD, PhD** retired on July 31, 2019. Dr. Johnson was the Associate Director of Research for the NW PADRECC, a basic scientist, and a clinician. During his time at OHSU and the VA, Dr. Johnson has conducted extensive research on the electrophysiology of dopaminergic neurons in the ventral tegmental area and basal ganglia in the mouse model. He has explored the functionality of various receptors, ion channels, and pharmacological agents on neuronal activity, as well as their implications for the treatment of neurological diseases.



Marian Dale, MD, MCR. Dr. Dale attended the University of Chicago for her BA in biology, obtained her MD at the Medical University of South Carolina in 2009, and completed her residency at the University of Maryland Medical Center in Baltimore MD. She trained as a Movement Disorders fellow with the NW Portland PADRECC from 2013 – 2015. She remained at Oregon Health & Science University until 2017. She moved to the Medical University of South Carolina as an assistant professor of neurology and will return to the Portland VA and OHSU in September of 2019 as a part-time clinician. Dr. Dale has research interest in TMS treatment for PSP (progressive supranuclear palsy).

Education Update

Support Groups: In the past fiscal year, Kristi Ketchum, LCSW has designed, implemented, and run a monthly support group for Parkinson's patients and their caregivers. The support group meets every second Friday of the month at the VA Portland.

Started at the end of 2018, Seattle Puget Sound has a support group that meets the second Friday of the month to coincide with the Movement Disorders Clinic, so they can visit the support group the same day as their appointment. Group leaders in Seattle are Jaci Girad and Tracy Broomhead, who are both registered nurses, with VTEL connection to the American Lake VA where Ann Gellenbeck is the group leader.

Outreach. Dr. Joseph Quinn, NW PADRECC Director, in conjunction with the Parkinson's Resources of Oregon (PRO), a local non-profit group travelled to Roseburg, Oregon for an educational event. Dr. Quinn gave a lecture to a very well attended mixed group of veterans and non-veterans.

Research Update

The NW PADRECC strongly encourages and supports investigator-initiated research projects.

Some *fellow-initiated* projects recruiting in the past year:

Describing the differences between disease process and treatment effect (ATAX; OHSU eIRB # 18608; VA MIRB # 4299). *Initiated by Dr. Jennifer Nichols, fellow 2017-2019, currently run by Dr. Venka Veerappan, fellow 2018-2020.* The study aims to characterize ataxia occurring in essential tremor and essential tremor with DBS.

Characterizing Biomarkers of Early Parkinson's Disease Progression (TREG; OHSU eIRB # 18545; VA MIRB 4277). *Initiated by Dr. Jill Baird, fellow 2017-2019, currently run by Dr. Lee Neilson, fellow 2019-2021.* The study aims to characterize the rate of change in a peripheral blood marker of inflammation (Treg percentage) and three quantitative motor measures (finger tapping, 9-hole peg test and peak turn velocity) in a cohort of 25 untreated PD patients.

Clinical Characteristics of Parkinson's Disease Subjects with Severe Hypertension During Motor OFFs (VA IRB # 4202). *Initiated by Dr. Christopher Way, fellow 2016-2018.* Dr. Kathryn Chung are conducting a research study looking at blood pressure changes in Parkinson's disease (PD).

Northwest PADRECC Update (continued)

Buspirone, in combination with amantadine, for the treatment of levodopa-induced dyskinesia (OHSU eIRB # 11875; VA MIRB # 3753). Initiated by Dr. Victoria Holiday, fellow 2014-2016. Dr. Kathryn Chung is conducting a research study looking at the effect and the safety (side effects) of buspirone in combination with amantadine on abnormal involuntary movements (dyskinesias) in Parkinson's disease (PD).

Some faculty-initiated projects recruiting in the past year:

STAT-PD: Preventing Levodopa Induced Dyskinesia in Parkinson's disease with HMG-CoA Reductase Inhibitors (OHSU eIRB # 17302; MIRB # 3869). VA CSR&D Merit Review Grant – in collaboration with Puget Sound VA. Dr. Kathryn Chung is conducting a research study looking at movements in Parkinson's disease (PD). In this study, we will examine the association of statin use and dyskinesia in a convenience sample Parkinson's disease patients in the Veterans Administration Health Care System.

Measuring Cortisol Levels in Persons with Parkinson's (PD) (VA IRB # 3794, OHSU eIRB # 15183). Dr. Amie Hiller is conducting a research study looking at cortisol levels in Parkinson's disease (PD), Huntington's disease (HD), and Healthy Controls (HC). Cortisol is a hormone that is normally released in response to events and circumstances such as waking up in the morning, exercising, and stress.

Pacific Northwest Udall Center (PaNuC): Clinical Core and Specimen Collection (VA IRB # 2332; OHSU eIRB # 6154). NIH UDALL Grant – in collaboration with Puget Sound VA. Dr. Joseph Quinn is conducting this research study to examine the changes in thinking and memory of Parkinson's disease patients over time. A second goal is to determine the role genetics plays in cognitive impairment in Parkinson's disease.

Publications: The present and past faculty, fellows, and staff of the NW PADRECC have continued to publish peer-reviewed journal articles, abstracts, and give lectures around the Pacific NW. Some notable publications by fellows and/or junior faculty include:

Mack, J., Quinn, J., Lobb, B. M., & O'Connor, S. (2019). Functional movement disorders in US veterans: Psychiatric comorbidity and health care utilization. *Movement Disorders*, 34(5): 755-6.

Seier, M., Hiller, A., Quinn, J., Murchison, C., Brodsky, M., & Anderson, S. (2018). Alternating thalamic deep brain stimulation for essential tremor: A trial to reduce habituation. *Movement Disorders Clinical Practice*, 5(6): 620-6.

Way, C., Pettersson, D., & Hiller, A. (2019). The 'Hot Cross Bun' sign is not always multiple system atrophy: Etiologies of 11 cases. *Journal of Movement Disorders*, 12(1):27-30.

Active Grants: The NW PADRECC currently has 10 Active Research Grants

San Francisco PADRECC Update

Clinical Update

Welcome New Providers!



Rafael Zuzuarregui MD
Movement Disorders & Sleep Specialist
Assistant Clinical Professor, UCSF

Dr. Zuzuarregui is board certified in Neurology and fellowship trained in both Movement Disorders and Sleep Disorders. Joining SF-PADRECC September 2019, Dr. Zuzuarregui is interested in the treatment of Parkinson's and Huntington's disease, as well as sleep disorders.

San Francisco PADRECC Update (continued)



Cameron Dietiker, MD
Movement Disorders Specialist
Assistant Clinical Professor, UCSF

Dr. Dietiker has joined SF-PADRECC (August 2019). Board certified in Neurology, Dr. Dietiker completed her Fellowship in Movement Disorders at PADRECC-San Francisco (SFVAHCS). We are happy to share her with UCSF Movement Disorders and Neuromodulation Center. Welcome Back!

Telehealth Expansion

Whether it is VA medical center to center, or directly to a Veteran's home (computer, laptop or hand-held device) if it is digital: the VA is providing Care. In our clinics, every room with a door now has the technology for extended outreach. Our PADRECC Fellows become experienced telemedicine providers during their terms with us and the VA/UCSF Resident Telehealth Program is a significant success in preparing new neurologists in providing care electronically.

Recently published article on the Resident Telehealth Program:

Education Research: An experiential outpatient teleneurology curriculum for residents.

<https://www.ncbi.nlm.nih.gov/pubmed/31332085>

Poster accepted at the American Academy of Neurology Annual Meeting (AAN), May 2019

"Global Teleneurology Service: First Insights"

PADRECC-San Francisco is well represented on the International Parkinson and Movement Disorder Society (MDS) Telemedicine Study Group: Maya Katz, Nicholas Galifianakis, Caroline Tanner (Director, PADRECC-SF), and Mitra Afshari, recently graduated PADRECC Fellow.

Supportive Care for Parkinson's Disease

Maya Katz, MD and Nicholas Galifianakis, MD, MPH at PADRECC San Francisco began clinics for advanced care for PD two years ago to address the important patient and care-partner focused communication, and multi-disciplinary approach needed in symptom management, advanced care planning and palliative care for PD.

Dr. Katz presented a poster at the 5th World Parkinson Congress (WPC) June 2019 Kyoto, Japan:

"Team-based outpatient palliative care improves patient and care partner-centered outcomes in Parkinson's disease"

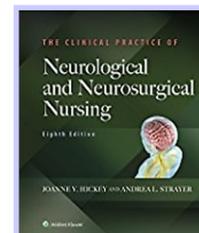
Dr. Galifianakis taught two courses at World Parkinson Congress (Kyoto) and will also present at International Congress of Parkinson's Disease and Movement Disorders (MDS) September 2019 Nice, France: *Palliative Care for Parkinson's Disease and Managing Palliative Needs of Patients and their Caregivers*. Dr. Galifianakis is the Chair, Palliative Care for Parkinson's Disease, for MDS.

Education Update

Books and Chapters:

[The Clinical Practice of Neurological and Neurosurgical Nursing, Eighth Edition](#)

Susan L. Heath, RN, MSN authored *Chapter 29: Parkinson's Disease* [Section 9: Nursing management of patients with movement disorders, neurodegenerative and neuromuscular diseases.] One of the originating members of the San Francisco PADRECC, Susan recently retired from SFVAHCS (29 yrs service) to join the Department of Neurosurgery, Neuroscience Institute at Evergreen Hospital, Kirkland, WA.



EES/PADRECC Movement Disorders Series: Parkinson's Disease-101 (Sept 12, 2019)

This well-attended webinar was an overview of PD why, what, where and how of current treatment by Ethan G. Brown, MD, Assistant Clinical Professor, University of California, San Francisco (UCSF). Dr. Brown completed his Advanced Fellowship Parkinson's Disease at PADRECC-San Francisco.

San Francisco PADRECC Update (continued)

Nursing Education Outreach:



Annie Li Wong, MSN, GNP-BC, movement disorders nurse practitioner partnered with Pharmacy, Geriatrics, Palliative and Extended Care nurses to identify areas for improvement for nursing home care of Parkinson's disease patients. Projects include developing PD education for Community Living Center (CLC) nurses, and other home nurses, with a focus on non-motor symptoms of PD. Annie has presented at San Francisco VAHCS' CLC; the Bay Area Nursing Care Conference at SFVAHCS; California Veterans Homes (CALVet) Fresno; and at VA Pacific Islands HCS, Honolulu. This important aspect of PD-education was acknowledged by the 5th World Parkinson Congress' acceptance of poster: "Bridging the gaps in Parkinson's education for nurses in long-term care facilities" June 2019 Kyoto, Japan. Annie, and her fellow nurses, expect to expand the reach of this sharing of PD-care information through continued site visits and enduring materials.

Research Update

Publications on Supportive Care for PD:

Framing advance care planning in Parkinson disease: Patient and care partner perspectives.

Neurology. 2019 May 28;92(22):e2571-e2579. doi: 10.1212 / WNL.0000000000007552. Epub 2019 Apr 26. PMID: 31028124
<https://www.ncbi.nlm.nih.gov/pubmed/31028124>

Does outpatient palliative care improve patient-centered outcomes in Parkinson's disease: Rationale, design, and implementation of a pragmatic comparative effectiveness trial.

Clin Trials. 2019 Apr;79:28-36. doi: 10.1016/j.cct.2019.02.005. Epub 2019 Feb 16. PMID: 30779960 <https://www.ncbi.nlm.nih.gov/pubmed/30779960>

Top Ten Tips Palliative Care Clinicians Should Know About Parkinson's Disease and Related Disorders.

Palliat Med. 2018 Oct; 21(10):1507-1517. doi: 0.1089/jpm. 2018.0390. PMID: 30204543
<https://www.ncbi.nlm.nih.gov/pubmed/30204543>

Neuropalliative care: Priorities to move the field forward.

Neurology. 2018 Jun 27. pii: 10.1212/WNL.0000000000005916. doi: 10.1212/WNL.0000000000005916. [Epub ahead of print] Review. PMID: 29950434 <https://www.ncbi.nlm.nih.gov/pubmed/29950434>

Publications on Telemedicine for PD:

Education Research: An experiential outpatient teleneurology curriculum for residents.

Neurology. 2019 Jul 23;93(4):170-175. <https://www.ncbi.nlm.nih.gov/pubmed/31332085>

The Promise of Telemedicine for Movement Disorders: An Interdisciplinary Approach.

Curr Neurol Neurosci Rep. 2018 Apr 13;18(5):26. 3 <https://www.ncbi.nlm.nih.gov/pubmed/29654523>

Telemedicine Use for Movement Disorders: A Global Survey.

Telemed J E Health. 2018 Mar 22. <https://www.ncbi.nlm.nih.gov/pubmed/29565764>

Selection of other 2019 Publications:

Magnetic resonance imaging-guided phase 1 trial of putaminal AADC gene therapy for Parkinson's disease. Ann Neurol. 2019 May;85(5):704-714 Epub 2019 Mar 26. PMID: 30802998 <https://www.ncbi.nlm.nih.gov/pubmed/30802998>
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6593762/>

Effect of levodopa on electroencephalographic biomarkers of the parkinsonian state.

J Neurophysiol. 2019 May 8. [Epub ahead of print] PMID: 31066605 <https://www.ncbi.nlm.nih.gov/pubmed/31066605>

San Francisco PADRECC Update (continued)

Cortical Basal Ganglia Network Interactions During Sequence Learning in Parkinson's Disease

Neurosurgery, Volume 66, Issue Supplement_1, September 2019, nyz310_369 https://doi.org/10.1093/neuros/nyz310_369

Longitudinal analyses of cerebrospinal fluid α -Synuclein in prodromal and early Parkinson's disease.

Mov Disord. **2019 Jul 30**. doi: 10.1002/mds.27806. [Epub ahead of print] PMID: 31361367 <https://www.ncbi.nlm.nih.gov/pubmed/31361367>

Patient Experience with Rechargeable Implantable Pulse Generator Deep Brain Stimulation for Movement Disorders.

Stereotact Funct Neurosurg. 2019 Jul 9:1-7. [Epub ahead of print] PMID: 31288242 <https://www.ncbi.nlm.nih.gov/pubmed/31288242>

Rotenone and Parkinson's disease: reduced sensitivity in females.

Toxicol Sci. **2019 Jun 4**. pii: kfz126. doi: 10.1093/toxsci/kfz126. [Epub ahead of print] No abstract available. PMID: 31161209 <https://www.ncbi.nlm.nih.gov/pubmed/31161209>

Southwest PADRECC Update

The VA Greater LA Health Care System is the hub for the center of excellence for the Southwest PADRECC. Providing subspecialty care to patients with Parkinson's Disease and other Movement Disorders, the center conducts evaluations and management of **Deep Brain Stimulation** for Parkinson's Disease, Essential Tremor, and Dystonia. The clinic also provides **Botulinum Injections** for various Parkinson related disorders, as well as providing **VA Video Connect (telehealth)** for our patients

Clinical Update

Integrative Medicine: This year Dr. Indira Subramanian, Director of Southwest PADRECC, has collaborated closely with the Integrative Medicine group at the VA Greater Los Angeles (VA GLA) to design a "Living Well with PD" clinic. Integrative Medicine considers the whole person, including all aspects of lifestyle. It emphasizes the partnership between provider and patient and makes use of all appropriate therapies.

Telehealth: Under the direction of Dr. Adrienne Keener, the Southwest PADRECC located in VA GLA is expanding access to care by integrating VA Video Connect into their clinical practice.

Neuro-Pharmacy Program: In collaboration with **Sunita Dergalust, PharmD**, integrated specialized pharmacy care in the PADRECC at the VA Greater LA. Patient records are reviewed to determine if a patient is compliant in refilling Movement Disorders related medications. If compliance is not met, a pharmacy resident will then call the patient to review dosing and assess for any barriers or concerns. Pharmacy residents also meet with patients during clinic to provide education and ensure they are taking their medication as prescribed.

Education Update

PD 101 Symposium Fall 2018: PD 101 is a course for patients and caregivers to give them basic information about PD and how they can take better care of themselves using the resources the VA provides. Dr. Keener presented on symptoms, Dr. Subramanian presented on treatments, Dr. Dergalust from Pharmacy talked about medications and compliance, and Dr. Feil spoke on non-motor issues in PD including mood and cognition.

Living Well with PD Symposium April 2019: This year the Living Well with Parkinson's Disease Symposium was introduced. This symposium is a 2-hour event held at the medical center. The Southwest PADRECC collaborated with VA staff members and the community to



Southwest PADRECC Update (continued)

present diverse topics related to PD. Some of the topics presented were mindfulness, yoga, physical therapy, exercise, dancing through Parkinson's, medications, mood, cognition and psychosis. Patients participated in a range of fun and beneficial activities including yoga, mindfulness, dance and exercise.

Women in PD: In 2018, Dr. Keener partnered with the Parkinson's Foundation as a Regional Team Leader for the Women and PD Teams to Advance Learning and Knowledge (TALK) initiative. The regional forum brought together health care providers, caregivers, stakeholders, and women with PD to discuss gender-specific issues in PD. Dr. Keener also participated in a national forum, contributing to the development of a patient-centered research and care agenda to address gender disparities in PD. <https://www.parkinson.org/expert-care/Expert-Care-Programs/Addressing-Womens-Needs/Women-and-PD-TALK>



PD at Home: The Southwest PADRECC hosts the PD at Home teleconference that is held the 2nd Tuesday of every month from 10:00 – 11:00 am PST, via toll free number 1.800.767.1750 code 5431# and is facilitated by Clinical Nurse Coordinator, **Patricia Pittman**. The PADRECC Education Committee seeks out speakers who present diverse topics on PD.

Research Update

Parkinson's Environment and Gene (PEG) Study: Adrienne Keener, MD is a study physician on this NIH-funded study of over 800 patients and 800 matched controls recruited to date. They have continued to recruit new subjects and controls through a recently funded grant from the NIEHS using the California Registry to identify new subjects. Five manuscripts have been published describing gene polymorphisms and progression of PD; more manuscripts have been submitted. Additional NIH funding is being requested to follow this cohort to determine genetic and environmental factors that alter progression of PD. Dr. Keener was the recipient of a pilot grant from the American Parkinson Disease Association to examine PD onset and progression phenotype in Hispanic participants of the PEG study. She conducts the assessments of new and follow-up study subjects and assists in data analysis.

Ketamine as treatment for PD dyskinesia: Dr. Scott Sherman, of the VA Tucson has been working to repurpose the anesthetic drug ketamine as a treatment for dyskinesia and non-motor symptoms of PD. They originally reported the clinical observations that low dose infusions of ketamine for a period of 72 hours led to sustained benefits in reducing levodopa-induced dyskinesia (LID). The doses used did not cause any significant side effects or sedation and had effects lasting several months. The next goal is to design a prospective, randomized, placebo-controlled Phase 2 clinical trial to further confirm this result. To properly design this trial, they have developed a pre-clinical rodent model of LID to predict the dose response, duration of response and mechanism of action of ketamine. They have found that shorter infusions (10 hrs. or less) in the sub-anesthetic range are still effective in the rodent model. If this translates to humans, then it may be feasible to use an abbreviated outpatient treatment regimen. In addition, they have made significant progress in understanding the mechanism of action of ketamine in this model system. They have found that ketamine acts to alter long-term oscillatory behavior of cortico-striatal circuits in manner analogous to Deep Brain Stimulation. They are also investigating the role of the neurochemical BDNF that is likely up-regulated by ketamine treatment. They have been successful this year in obtaining funding from the Arizona Biomedical Research Council (750,000 over 3 years to conduct this research).

Glycopeptide Agonists as Neuroprotective Therapies for Parkinson's Disease. Dr. Sherman's VA Tucson basic research laboratory is a major collaborator on an NIH funded project to develop neuro-protective molecules in rodent models of PD. NINDS (1 R01 NS 091238-01A1, 09/30/15 to 06/30/20, PACAP/VIPV).

Southwest PADRECC Update (continued)

Southwest PADRECC/Consortium Update

VA Loma Linda Health Care System: Dr. Dorothee Cole manages the movement disorders clinic at the VA in Loma Linda, CA, which provides specialty care for patients with PD including DBS programming, Duopa pump programming and Botulinum toxin therapy. In addition, she treats other movement disorders such as myoclonus, tremor, Huntington's disease, and ataxia. She provides teaching to medical students, neurology residents, and clinical pharmacy residents.

VA San Diego Health Care System: Dr. Caitlin Mulligan joined San Diego VA in August. Dr. Mulligan along with **Dr. Stephanie Lessig** serve as attending neurologists in weekly Movement Disorders Clinics and Botulinum toxin clinics at the VA San Diego Health Care System - La Jolla, CA.

Dr. Lessig is the Co-Principal Investigator at UCSD for the nationally recognized PPMI study by the Michael J Fox Foundation that targets newly diagnosed Parkinson's patients throughout the community, including the VA. Dr. Lessig collaborates extensively with the Neuropsychology department at VA San Diego and participates in many protocols analyzing cognition in Parkinson's. She is Co-Investigator on the protocol "Investigating Exercise-Induced Neuroplasticity and its Mechanisms in Parkinson's Disease: Targeting Executive Function and Brain Circuitry".

New Mexico (Albuquerque) VA Health Care System: Dr. Sarah Pirio-Richardson, a movement disorders specialist, and **JoAnn Harnar, RN** run the PADRECC clinic in Albuquerque, New Mexico. Clinical activities include specialty care for patients with tremor, ataxia, PD and dystonia. Botulinum toxin injections and deep brain stimulation programming are done for patients in VISN 18 from Eastern Arizona, Southern Colorado, New Mexico and Western Texas. Teleneurology and nurse education sessions are important parts of these services.

Las Vegas VA Health Care System: Dr. Selina Parveen provides movement disorder, DBS and botulinum toxin management to a large catchment area in Nevada, Arizona and Utah in VISN 22. She is often a guest speaker at the community support group, Friends of Parkinson's, in which many Veterans attend. She is teaching the medical students at UNLV school of medicine. She also has academic affiliation at Touro Medical College.

Southern Arizona (Tucson) VA Health Care System: Scott Sherman, MD, PhD and his research laboratory focus on developing novel therapies for PD and have several translational research projects. His research led to the discovery that neurotrophic factors, Vascular Endothelial Growth Factor-B and a PEDF, a factor derived from the retina, are neuro-protective. Basic laboratory studies in these areas are continuing. Another line of research explores the use of low-dose ketamine for the treatment of PD dyskinesia. Preclinical work in the laboratory has shown that low-dose ketamine can prevent the development of dyskinesia in an animal model of PD. Recent human studies have shown that ketamine given at low doses can improve depression and pain. These findings open the door to study the potential of low-dose ketamine treatment for patients with PD that have dyskinesia, neuropathic pain, and depression, all of which are common comorbidities. Plans are underway to begin a small clinical trial next year.

VA Long Beach Health Care System: Dr. Steven Schreiber is Chief of Neurology at the VA Long Beach Health Care System where he oversees the local PADRECC and was instrumental in developing the first Teleneurology programs in the VA system. **Dr. An Tran**, a Movement Disorders Specialist, runs a botulinum toxin clinic and a Movement Disorders/DBS clinic. She enjoys teaching neurology and psychiatry residents. Also, Dr. Tran likes to be involved in community outreach programs and is a guest speaker at community support groups and VA Long Beach Parkinson Support Group. **Megan Gomez, PhD**, a licensed clinical psychologist in the Primary Care Mental Health Integration Clinic, who specializes in neuropsychology and neurodegenerative diseases, facilitates a monthly Parkinson's Support Group at the VA Long Beach.

National VA PD Consortium Center Updates

Richmond PADRECC

Ralph H. Johnson VA Medical Center, Charleston, SC

Christine Cooper, MD

Vanessa Hinson, MD PhD

Changes in structural connectivity in Vascular Parkinsonism: Using diffusion kurtosis imaging magnetic resonance imaging, Drs. Christine Cooper, Vanessa Hinson, and collaborators from the Medical University of South Carolina found decreased structural connectivity selectively within the basal ganglia motor loop in subjects with Vascular Parkinsonism (VP), compared to clinical cohorts of Parkinson's disease and healthy aging subjects. Whole brain connectome fiber counts in VP subjects strongly correlated with clinical ratings scores of gait and balance. Future studies will further investigate potential explanations for these changes in circuitry in VP. This work was also supported by the National Institutes of Health (KL2 TR001452 & UL1 TR001450, 15SFDRN-26030003, 15SFDRN-25870000), and the MUSC Foundation: Barmore Fund, Charleston, SC

Philadelphia PADRECC

James J. Peters VA Medical Center, Bronx, NY

Director: Ruth Walker, MD

Melissa J. Nirenberg, MD, PhD recently joined the James J. Peters VA Medical Center PADRECC Consortium Center in the Bronx, where she will be working with Dr. Ruth Walker in the Movement Disorders Clinic, in addition to helping expand the telemedicine resources for movement disorders. Dr. Nirenberg is a Clinical Professor of Neurology at the Icahn School of Medicine at Mount Sinai and fellowship-trained movement disorders specialist who brings with her an extensive background in research, teaching, and patient care related to Parkinson's disease and other movement disorders. Dr. Nirenberg has a particular research interest in impulse control disorders and other non-motor manifestations of Parkinson's disease, and discovered, named, and published the first report of dopamine agonist withdrawal syndrome (DAWS) in the literature. She has been strongly involved in education related to Parkinson's disease, including patient and caregiver outreach, house staff training, and CME courses. Dr. Nirenberg completed her MD/PhD at Weill Cornell, residency training in neurology at the University of California, San Francisco, and fellowship training in movement disorders at Columbia University. She was most recently on faculty at NYU Langone, where she was also Associate Director of the neurology residency program. Dr. Nirenberg enjoyed working with veterans at the San Francisco VA Medical Center PADRECC during her residency training, and is excited to have the opportunity to work with veterans once again as part of the PADRECC Consortium

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 National Coordinator for Operations

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Northwest	Portland VAMC VA Puget Sound Health Care System	Portland, OR Seattle, WA	Joe Quinn, MD	Portland: 503-721-1091 Seattle: 206-277-4560
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Southeast	Hunter Holmes McGuire VAMC	Richmond, VA	Jessica B. Lehosit, DO	804-675-5931 or toll free 800-784-8381 ext 5931
San Francisco	San Francisco VAMC	San Francisco, CA	Caroline Tanner, MD	415-379-5530

